*Editorial*

# Angiographic assessment of myocardial perfusion: TIMI myocardial perfusion (TMP) grading system

Since the introduction of reperfusion therapy in the early 1980s, cardiologists have largely focused on coronary artery flow and diameter, with the goal being to restore normal epicardial artery perfusion and large lumens. For many years, epicardial coronary flow has been simply assessed by the TIMI (thrombolysis in myocardial infarction) flow grade.[1] This semiquantitative coronary angiographic tool places a patient's coronary flow into one of four different categories and has been shown to be associated with mortality. The corrected TIMI frame count provides a more objective quantitative index of coronary flow and has been shown to segregate even TIMI grade 3 flow into lower and higher risk subgroups.[2–4]

It is becoming increasingly clear that tissue perfusion, not just an open artery, is critical to myocardial salvage. For instance, among all patients with "open arteries" (TIMI grade 2 or 3), those with TIMI 2 flow have a higher mortality, probably as a result of impaired microcirculation.[5] Myocardial contrast echocardiography demonstrates impaired microvascular flow among TIMI grade 2 patients, and even those with TIMI 3 flow after primary percutaneous transluminal coronary angioplasty (PTCA) have a poor recovery if there is no perfusion by this method.[6] Impaired microvascular perfusion in the presence of open epicardial coronary arteries is thought to be caused by downstream microvascular obstruction, α adrenergic neural reflexes, spasm or thrombotic occlusions of microvessels.[7]

**Establishing a perfusion grading system**

Just as the TIMI flow grades are important to studies of coronary artery flow, establishing a myocardial perfusion grading system is important to standardise studies of myocardial perfusion. A number of methods have been used to assess myocardial perfusion such as myocardial contrast echocardiography, thallium/sestamibi myocardial perfusion imaging, and coronary flow reserve measurement. Recently, coronary angiography has been used to assess myocardial perfusion by the measurement of dye passing into and out of the myocardium which is evident as a ground glass appearance, or "blush."[8] Adequacy of tissue perfusion can be graded by quantifying this blush using conventional dye and angiographic techniques.

Perfusion of the myocardium can be categorised using the TIMI myocardial perfusion (TMP) classification system.[8] In TMP grade 3, there is the normal diffuse ground glass appearance of myocardial blush. At the end of the washout phase, dye is only mildly persistent or gone. The washout phase is the time after the end of dye injection during which dye would normally be expected to clear from the epicardial vessels during opacification of the myocardium, followed by clearing from the myocardium. In TMP grade 2, dye enters the myocardium, but accumulates and exits more slowly, so that at the end of the washout phase dye in the myocardium is strongly persistent; however, dye totally clears by the next injection. In TMP

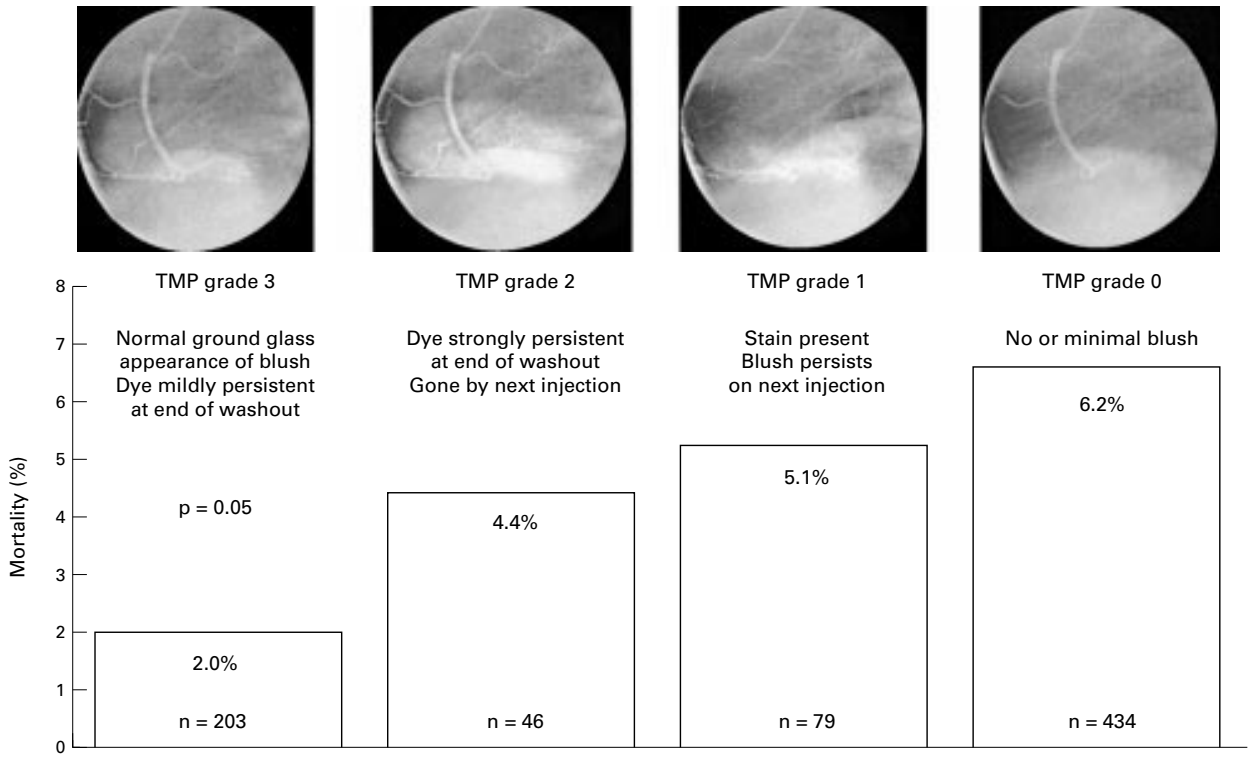


*Figure 1 TIMI myocardial perfusion (TMP) grades.*[8]

grade 1, the dye does not leave the myocardium and there is a stain on the next injection. In TMP grade 0, dye does not enter the myocardium and there is minimal or no blush apparent during the injection and washout phases. Static pictures of the TMP grades are shown in fig 1, but more informative cine-loops and training are available at the angiographic core lab web site (www.perfuse.org).

Angiographic assessment of myocardial perfusion is a simple technique that can be undertaken in any analogue or digital laboratory at the time of the procedure without the need for specialist equipment. While simple and broadly applicable, attention to several simple technical issues is necessary if accurate, reproducible angiographic assessments of myocardial perfusion are to be made. Assessment of the size and intensity of myocardial blush may vary according to the view selected. It is therefore important to specify the precise view used for acquiring images. The optimal angiographic views are carefully chosen to avoid vessel overlap. Suitable views would usually be: left anterior oblique with cranial tilt for the right coronary artery; the right anterior oblique view with caudal tilt for the circumflex artery; and the right anterior oblique with cranial tilt for the left anterior descending coronary artery. Imaging is continued for at least three cardiac cycles in the washout phase (after dye has cleared from the epicardial vessels). Assessment of myocardial perfusion is made during mid-diastole, as this is the time at which the perfusion blush is at its most intense. Blush is easiest to identify by comparing images before and after the dye reaches the myocardium. This is facilitated by not panning during the filming and by using 9 inch image intensifier mode. The present data on TIMI myocardial perfusion grading relate to assessment before and after revascularisation strategies. Efforts are being made to look at the time course of the measurements and to calculate the intra- and interobserver variability of the technique.

## Clinical importance of TMP grading

The clinical importance of the TMP grading system is demonstrated by the ability to provide independent risk stratification among patients with normal epicardial TIMI grade 3 flow. Although the goal of revascularisation strategies is to restore TIMI grade 3 flow to the epicardium, it appears that myocardial perfusion is also important to improve mortality. Even among patients with epicardial TIMI grade 3 flow, there is an eightfold difference in mortality depending upon whether the patient has normal myocardial perfusion (TMP grade 3) versus a closed myocardium (TMP grade 0/1).[8] In patients with normal flow in the epicardial artery, those with TMP grade 0/1 have a 5.4% mortality, compared with a mortality of 2.9% in TMP grade 2, and a mortality of 0.7% in TMP grade 3. Thus, the TMP grading system offers prognostic information independent of the TIMI epicardial flow grades. TMP grade was shown to be a multivariate predictor of mortality independent of age, sex, pulse at admission, anterior myocardial infarction location, TIMI frame count or TIMI flow grade.[8] Finally, TMP grade remains an independent predictor of mortality even two years after thrombolytic treatment.[9]

While the previous data were obtained in the setting of thrombolysis, similar associations have been observed following percutaneous intervention in acute myocardial infarction.[10] Thirty day mortality in the presence of normal epicardial (TIMI 3) flow and normal myocardial perfusion (TMP grade 3) was 4.3%, compared with a mortality of 12.2% in normal epicardial (TIMI 3) flow but impaired myocardial perfusion (TMP grade 0/1). High risk patients with TIMI 3 flow following primary or rescue PTCA also have greatly improved outcomes in TMP grade 3 compared with grade 0/1.[11] TMP grade assessment is an independent predictor of mortality. Myocardial perfusion grading also predicts regional and global wall motion index at four weeks following primary PTCA and stent placement.[12]

Recently, Lepper and colleagues have shown that tissue level perfusion as assessed by angiographic myocardial blush grade relates to coronary flow reserve, myocardial contrast echo, and wall motion abnormalities.[12] Thus, this simple angiographic technique is related to other techniques used to assess the integrity of the microvasculature. Studies comparing angiographic perfusion grading with positron emission tomographic scanning or isotope perfusion imaging are yet to be undertaken.

While the visually assessed TMP grades are clinically useful, efforts are currently underway to characterise tissue level perfusion more quantitatively using digital subtraction angiography. In this method, subtraction of the image of the vessel filled with contrast from an equivalent image several cardiac cycles later, complete with the blush, results in an image of only the myocardial blush. This technique requires the use of digitally acquired images and a software analysis program to generate the "blush image". By careful technique acquiring digital images in 9 inch mode without panning, promising results are being obtained using software analysis for the offline quantification of myocardial blush.

Myocardial perfusion can be assessed simply through the use of angiographic techniques such as the TMP grading system. This broadly applicable method can easily be undertaken during clinical angiography, and may facilitate both the clinical and research assessment of tissue level perfusion.

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